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Health and Environmental
Effects Profile for Ronnel

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HEALTH AND ENVIRONMENTAL EFFECTS PROFILE
FOR RONNEL

ENVIRONMENTAL CRITERIA AND ASSESSMENT OFFICE
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16. ABSTRACT The Health and Environmental Effects Profile for <u>Ronnel</u> was prepared by the Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office, Cincinnati, OH for the Office of Solid Waste to support listings of hazardous constituents of a wide range of waste streams under Section 3001 of the Resource Conservation and Recovery Act (RCRA). Both published literature and information obtained from Agency program office files were evaluated as they pertained to potential human health, aquatic life and environmental effects of hazardous waste constituents. Quantitative estimates have been presented provided sufficient data are available. <u>Ronnel</u> has been determined to be a systemic toxicant. An Acceptable Daily Intake (ADI), defined as the amount of a chemical to which humans can be exposed on a daily basis over an extended period of time (usually a lifetime) without suffering a deleterious effect, for <u>Ronnel</u> is 5×10^{-2} (mg/kg bw/day) for oral exposure.			
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PREFACE

Health and Environmental Effects Profiles (HEEPs) are prepared for the Office of Solid Waste by the Office of Health and Environmental Assessment. The HEEP's are intended to support listings of hazardous constituents of a wide range of waste streams under Section 3001 of the Resource Conservation and Recovery Act (RCRA). Both published literature and information obtained from Agency program office files are evaluated as they pertain to potential human health, aquatic life and environmental effects of hazardous waste constituents. The literature searched and the dates of the searches are included in the section titled "Appendix: Literature Searched."

Quantitative estimates are presented provided sufficient data are available. For systemic toxicants, these include, Acceptable Daily Intakes (ADIs) for chronic exposures. An ADI is defined as the amount of a chemical to which humans can be exposed on a daily basis over an extended period of time (usually a lifetime) without suffering a deleterious effect. In the case of suspected carcinogens, ADIs are not estimated in this document series. Instead, a carcinogenic potency factor or q_1^* is provided. These potency estimates are derived for both oral and inhalation exposures where possible. In addition, unit risk estimates for air and drinking water are presented based on inhalation and oral data, respectively.

The first draft of this document was prepared by Syracuse Research Corporation under EPA Contract No. 68-03-3228. The document was subsequently revised after reviews by staff within the Office of Health and Environmental Assessment: Carcinogen Assessment Group, Reproductive Effects Assessment Group, Exposure Assessment Group, and the Environmental Criteria and Assessment Office in Cincinnati.

The HEEP's will become part of the EPA RCRA docket.

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TABLE OF CONTENTS

	<u>Page</u>
1. INTRODUCTION.	1
1.1. STRUCTURE AND CAS NUMBER	1
1.2. PHYSICAL AND CHEMICAL PROPERTIES	1
1.3. PRODUCTION DATA.	2
2. ENVIRONMENTAL FATE AND TRANSPORT DATA	3
3. EXPOSURE-MONITORING	5
4. PHARMACOKINETICS.	6
4.1. ABSORPTION	6
4.2. DISTRIBUTION	6
4.3. METABOLISM	7
4.4. EXCRETION.	8
5. EFFECTS	9
5.1. CARCINOGENICITY.	9
5.2. MUTAGENICITY	9
5.3. TERATOGENICITY	9
5.4. OTHER REPRODUCTIVE EFFECTS	10
5.5. CHRONIC TOXICITY	10
5.6. OTHER RELEVANT INFORMATION	13
6. AQUATIC TOXICITY.	15
6.1. ACUTE TOXICITY	15
6.2. CHRONIC EFFECTS.	17
6.3. PLANT EFFECTS.	17
6.4. RESIDUES	17
6.5. OTHER RELEVANT INFORMATION	17
7. EXISTING GUIDELINES AND STANDARDS	18
7.1. HUMAN.	18
7.2. AQUATIC.	18
8. RISK ASSESSMENT	19
9. REFERENCES.	21
APPENDIX: LITERATURE SEARCHED.	28

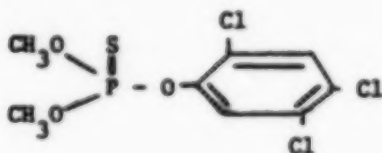
LIST OF ABBREVIATIONS

ADI	Acceptable daily intake
BCF	Bioconcentration factor
bw	Body weight
EC ₅₀	Median effective concentration
LD ₅₀	Dose lethal to 50% of recipients
NOAEL	No-observed-adverse-effect level
NOEL	No-observed-effect level
OSHA	Occupational Safety and Health Administration
ppm	Parts per million
SCE	Sister chromatid exchange
TLV	Threshold limit value
TWA	Time-weighted average

1. INTRODUCTION

1.1. STRUCTURE AND CAS NUMBER

Ronnel is the common name for the 0,0-dimethyl 0-(2,4,5-trichlorophenyl) ester of phosphorothioic acid. It is also known as fenchlorofos and violene. This compound was introduced in 1954 by the Dow Chemical Company under the trade names "Nankor", "Trolene" (drug grade) and "Korlan" (technical grade), and the code numbers "DOWET-57" (drug grade) and "DOWET-14" (technical grade) (BCPC, 1977). The structure of ronnel is depicted below:



Molecular formula: $C_8H_8Cl_3O_3PS$

Molecular weight: 321.5

The Chemical Abstracts Service (CAS) Registry Number for this compound is 299-84-3.

1.2. PHYSICAL AND CHEMICAL PROPERTIES

Ronnel is a white crystalline powder. It is soluble in most organic solvents and stable at temperatures up to 60°C in neutral and acidic media (BCPC, 1977). Some of the physical properties are listed below:

Boiling point:	97°C at 0.01 mm Hg (Freed et al., 1977)
Melting point:	40-42°C (BCPC, 1977)
Vapor pressure:	8×10^{-4} mm Hg at 25°C (BCPC, 1977) 5.3×10^{-5} mm Hg at 20-25°C (Freed et al., 1979)
Water solubility:	40 mg/l (BCPC, 1977)
Calculated BCF (fish):	340 (Kenaga, 1980a)

Estimated soil sorption coefficient (K_{oc}):	1600 (Kenaga, 1980b)
Octanol/Water partition coefficient (K_{ow}):	75,266-75,300 (Freed et al., 1976 1977, 1979)
Log K_{ow} :	4.88 (Chiou et al., 1977)

1.3. PRODUCTION DATA

Ronnel, an organophosphous insecticide, was produced by Dow Chemical Company in Midland, Michigan up to 1982 (SRI, 1982); however, no manufacturer of ronnel was located in the 1983 SRI Directory of Chemical Producers. United States production by Dow Chemical Company was reported as 2 million pounds/year for 1976 (Chemical Economics Handbook, 1976).

Ronnel is prepared by the reaction of O-2,4,5-trichlorophenyl phosphorodichloridothioate (made from sodium 2,4,5-trichlorophenolate and thiophosphoryl chloride) with sodium methylate in methanol (BCPC, 1977).

Ronnel is an insecticide. When applied as a spray, a pour-on liquid, a dip or a shampoo, ronnel controls ectoparasites of domestic animals (BCPC, 1977). Ronnel may also be used as a residual spray for the control of household pests.

2. ENVIRONMENTAL FATE AND TRANSPORT PROCESSES

Pertinent data regarding the fate and transport of ronnel in the atmosphere were not located in the available literature.

The fate of ronnel in water is likely to be determined by its ability to undergo chemical, photochemical and microbial degradation. The hydrolytic stability of this compound has been well studied. Ruzika et al. (1967) reported a half-life of 10.4 hours at pH 6.0 at 70°C (ethanol and water, 20:80) and Cowart et al. (1971) found that 95.1% (~5 half-lives) of ronnel was hydrolyzed within 1 week at pH 6.0 in distilled water. Pertinent data regarding the significance of microbial degradation or photochemical reactions in water were not located in the available literature.

The transport of ronnel in water will be influenced in part by its physical properties. Its relatively low water solubility (40 mg/l) suggests that the compound will be significantly adsorbed to soil particles or sediment. The extent of absorption will depend on the nature of the suspended particles and the temperature (Freed et al., 1977). Kenaga (1980b) predicted a soil sorption coefficient of 1600 from its water solubility, a value that indicates that ronnel will bind tightly to organic matter, and if the compound is applied to soil it is more likely to enter the water on eroded soils. The octanol/water partition coefficient (K_{ow}) of 75,300 ($\log K_{ow} = 4.88$) (Freed et al., 1976, 1977) and a calculated BCF of 340 ($\log BCF = 2.53$) measured in fish (Kenaga, 1980a) suggest that ronnel may bioaccumulate somewhat in aquatic organisms. Although no specific data were located, the relatively low vapor pressure of this compound (8×10^{-4} mm of Hg at 25°C) suggests that volatilization from water is not likely to occur.

The fate of ronnel in the soil has not been well studied. Data regarding the hydrolysis of ronnel in water (Ruzika et al., 1967; Plapp and

Casida, 1958; Cowart et al., 1971) indicates that chemical reactions may be a significant process for removal of this chemical in water; however, no specific data regarding these processes in soil were located in the available literature. No pertinent studies regarding the significance of microbial degradation or photolysis reactions of ronnel in the soil were located. Data supplied by Siddaramappa et al. (1973), however, have indicated that microorganisms in soils degraded organophosphates by cleavage of the P-O-C bond. Although ronnel was not studied specifically, it is possible that biological transformation of this compound by microorganisms may occur by the same process.

The transport of ronnel in the soil will be influenced by the process of leaching and volatilization. Based on the compound's high sorption coefficient [1600, predicted from its water solubility (Kenaga, 1980b)] and its relatively low vapor pressure (8×10^{-4} mm Hg at 25°C), it is unlikely that this compound will significantly leach or volatilize from the soil.

. 3. EXPOSURE-MONITORING

The Food and Drug Administration (FDA) reported that a residue level of 0.002 ppm of ronnel was present in toddler diets (specifically meat, fish and poultry) analyzed during 1975-1976 (Johnson et al., 1981a). A similar market-basket analysis for adult diets (specifically meat, fish, poultry, grain and cereal products) revealed residue levels of 0.002-0.006 ppm analyzed during 1975-1976 (Johnson et al., 1981b).

Monitoring data for ronnel available in STORET contained observations for 209 stations. The overall analysis revealed a range of 0.001-1.0 $\mu\text{g/l}$ with a mean of 0.33 $\mu\text{g/l}$ (n=640) for whole water samples, a range of 10.0-50.0 $\mu\text{g/kg}$ with a mean of 49.2 $\mu\text{g/kg}$ (n=140) for sediment samples (dry weight), and a level of 0.05 mg/kg for eight samples of aquatic animal tissue (wet weight) from ambient stream water.

4. PHARMACOKINETICS

4.1. ABSORPTION

No studies examining the absorption of ronnel were located in the available literature; however, it can be inferred from the metabolism study of Bradway et al. (1977) in rats and two abstracts of Polish metabolism studies in rats (Palut and Gryzmala, 1971) and rabbits (Zasadowski, 1981) that ronnel is absorbed from the gastrointestinal tract of both species of animals following oral administration.

4.2. DISTRIBUTION

Bradway et al. (1977) administered 37.3 mg/day (~216 mg/kg/day based on reported weights of 160-185 g) of ronnel by gavage to male Sprague-Dawley rats over a 3-day period, and found residues of the intact compound in the blood (0.36 ppm) on day 3, but none on day 8. The level of residue in the adipose tissue declined sharply from 370 ppm on day 3 to 0.40 ppm on day 8. Two abstracts of Polish studies described the distribution of ronnel in rats and rabbits. Approximately 6 hours after oral administration of 10 mg/kg of ³²P-labeled ronnel to rats, 3% of the radiolabel was detected in the liver, 1% in the kidneys and 0.1% in the brain. The maximum levels of ³²P in the blood occurred at 9 hours and trace amounts of ³²P persisted in the brain and blood at 72 hours (Palut and Grzymala, 1971). It was reported in an abstract of a Polish study that 1 month after a single dose of 0.25 mg/kg ronnel was administered orally to rabbits, 3.14 mg/kg was detected in the adipose tissue and kidney, 0.12 mg/kg was detected in the blood and 0.1 mg/kg in the liver (Zasadowski, 1981). It was not clear from the abstract whether the residues were parent compound or metabolites, but the presence of the trichlorophenyl ring was considered to be important for the prolonged retention.

4.3. METABOLISM

Bradway et al. (1977) administered ronnel by gavage at doses of 37.3 or 3.73 mg/rat/day every 24 hours for 3 days to male Sprague-Dawley rats. Urine from two rabbits/dose was pooled. The total amounts of ronnel administered to the pairs of rabbits over 3 days were 69.6 and 696 μ moles. The urine was collected after each day for 10 days and analyzed for alkyl phosphate metabolites and phenol metabolites. At both dose levels, the alkyl phosphate metabolites detected in the urine were 0,0-dimethyl phosphoric acid (DMP) and 0,0-dimethyl phosphorothioic acid (DMTP). At the high dose, a total of 52.1 μ moles of DMP and DMTP were excreted, accounting for 7.5% of the total dose. At the low dose, 9.81 μ moles of DMP and DMTP were excreted and accounted for 14.1% of the total dose. The 2,4,5-trichlorophenol recovery in the urine was 284 μ moles at the high dose and 32.6 μ moles at the low dose, with 40.8 and 46.9% of the total dose accounted for, respectively.

Plar $\ddot{u}$ and Casida (1958) administered ^{32} P-labeled ronnel to male and female rats at doses of 2 or 100 mg/kg by gavage dissolved in acetone and corn oil. Greater than 99% of the radioactivity recovered from the urine was in the form of water-soluble hydrolysis products. The proportion of alkyl-phosphate hydrolysis was much greater at the 100 mg/kg dose than at the 2 mg/kg dose and the proportion of oxidized derivatives was greater at the lower dose than at the higher dose.

In in vitro studies with rat, guinea pig and monkey liver homogenate, Rao and McKinley (1969) observed metabolism of ronnel when under conditions which favored oxidative desulfuration and reduced glutathione demethylation. Oxidative metabolism was sharply decreased or eliminated when nicotinamide or the cofactors NAD and NADP were omitted from the reaction mixture. The

rat, guinea pig and monkey liver homogenates appeared to be uniformly active in metabolizing this compound in both the oxidative and demethylating system.

4.4. EXCRETION

Bradway et al. (1977) reported that excretion of the urinary metabolites in rats was essentially complete within 48 hours after oral administration of 348 or 34.8 μ moles of ronnel (total amount given over 3 days).

In an abstract of a Polish study, Palut and Grzymala (1971) indicated that following oral administration of 10 mg/kg ^{32} P-labeled ronnel to rats, 74.5% of the radioactivity was eliminated within 24 hours, with 60.5% detected in the urine and 14.0% measured in the feces.

5. EFFECTS

5.1. CARCINOGENICITY

Pertinent data regarding the carcinogenicity of ronnel were not located in the available literature. This chemical is not scheduled for testing by the National Toxicology Program (NTP, 1983).

5.2. MUTAGENICITY

Ronnel gave no mutagenic responses in the in vitro "spot test" with Salmonella typhimurium (strains TA1535, TA1536, TA1537, TA1538), both in the presence and absence of metabolic activation (Carere et al., 1978). Ronnel also failed to induce point mutations in Streptomyces coelicolor [strains his A1 and A3(2)]. No concentrations were reported for this study. In an abstract of a Polish study, Szarapinska-Kwaszewska and Rozalska (1982) reported that ronnel failed to show any mutagenic activity in a reverse mutation assay with S. typhimurium in the presence or absence of the metabolic activating fraction.

Sobti et al. (1982) reported that ronnel produced a dose dependent increase in SCE in cultured human lymphoid cells (LAZ-007) in vitro at concentrations of 0.02, 0.2, 2 and 20 $\mu\text{g/ml}$ with significance at $p=0.01$ reported at the two highest concentrations.

5.3. TERATOGENICITY

In a teratogenicity study reported in an abstract by Khera et al. (1981), Wistar rats were treated by gavage with technical grade ronnel suspended in corn oil at doses of 0, 400, 600 or 800 mg/kg/day on days 6-15 of pregnancy. The dams were killed on the last day of pregnancy and the fetuses were evaluated. The authors noted that an increased incidence of extra ribs was observed in fetuses of all groups treated with ronnel. This increase appeared to be dose-related.

5.4. OTHER REPRODUCTIVE EFFECTS

Abstracts of two studies described the reproductive effects of ronnel in rats. Lactating rats were fed 4 mg/kg ronnel for the first 14 days of lactation. No significant statistical differences were observed in average carcass weights of pups from the treated group when compared with controls (Trankina et al., 1982a,b).

In an abstract of a Polish study, ronnel fed to rats at a dose level of 263 mg/kg on the last 7 days of pregnancy caused a depression in cytochrome oxidase and succinate dehydrogenase activities of brain mitochondria in the offspring when measured during the first 12 days of postnatal life. The author noted that these effects were associated with retardation of development and disturbance in phospholipid synthesis (Zalewska, 1980).

5.5. CHRONIC TOXICITY

Worden et al. (1972) administered ronnel in the diet at doses of 1, 3 or 10 mg/kg/day to groups of 3 male and 3 female Pembroke Shire Corgi dogs for 2 years and groups of 1 male and 1 female dog for 1 year. No overt clinical signs that could be associated with the administration of ronnel were observed in any of the treated animals during the 2-year period. Body weight did not appear to be affected even at the highest dose level of 10 mg/kg/day. There was no evidence of any significant effect on urinalysis, hematologic or histologic (52-week study) parameters, blood biochemistry, organ weights (52-week study), erythrocyte cholinesterase or brain cholinesterase. There was, however, an immediate effect on plasma cholinesterase activity in the 10 mg/kg/day group, and to a lesser extent in the 3 mg/kg/day group. The 10 mg/kg/day dietary group had plasma cholinesterase activities consistently below the controls ($p=0.01$) and the 3 mg/kg/day dietary group had activities that, on 50% of the occasions tested, were

below those of the control group ($p < 0.05$). The authors identified a NOEL of ronnel in dogs of 3 mg/kg/day, since the slight depression in plasma cholinesterase activity of this group was generally within a 20% variation from pre-treatment values and did not appear to be of practical significance. The 10 mg/kg/day dosage level, which produced no effects other than a depression of plasma cholinesterase activity, constitutes a NOAEL.

No adverse effects were observed in a female dog following administration of 25 mg/kg/day ronnel in the feed for 11 months (McCollister et al., 1959). Plasma, red cell and brain cholinesterase activity were found to be 29, 58 and 25% of normal, respectively. Following this initial study, female beagle hounds (one dog/dose) were fed 1000, 300, 100, 30 or 10 ppm of ronnel (average consumption of 25, 10, 3, 1 or 0.3 mg/kg/day) for 1 year without any significant adverse effects on growth, hematological parameters, organ weights, or terminal blood urea nitrogen. No evidence of detrimental effects was found upon microscopic examination of the tissues in any of the treated groups, and no significant changes in plasma or red blood cell cholinesterase activities were observed in the 3, 1 or 0.3 mg/kg/day groups (McCollister et al., 1959). Plasma cholinesterase was reduced to 45 and 29% of the control value at 10 and 25 mg/kg/day, respectively.

Groups of male and female rats were fed diets containing ronnel such that the dosage was 50, 15, 5, 1.5 or 0.5 mg/kg/day (McCollister et al., 1959). In the subchronic portion of the study, groups of 10 males and 10 females were fed the above dosages for 105 days; groups of 5 males and 5 females received the same treatment and then were returned to control diet for 1-2 months before being killed. In the chronic portion of the study, groups of 20 males and 20 females were fed the above dosages for 2 years;

additional groups of 10 males and 10 females were used for interim sacrifices at 1 year and 18 months. Results of the 105-day study revealed no significant adverse effects in the groups receiving 15, 5, 1.5 or 0.5 mg/kg/day ronnel when compared with the controls. In the 50 mg/kg/day group, however, there was some evidence in the liver of a slight granular degeneration of the parenchymal cells of the entire lobule. In the kidneys, there appeared to be swelling and vacuolation of the renal tubular epithelium with very slight interstitial nephritis. Similar changes were observed in the control animals, but in the opinion of the authors, to a different degree (McCollister et al., 1959). These differences were no longer apparent in the 50 mg/kg/day group that was allowed a recovery period.

The groups of rats maintained for 2 years on diets that delivered 50, 15, 5, 1.5 or 0.5 mg/kg/day of ronnel appeared physically normal and no significant differences were observed in growth, mortality or hemotological parameters when compared with the control groups. Microscopic examination of the livers of the 50 mg/kg/day group revealed evidence of centrilobular granular degeneration and some necrosis of the parenchymal cells. In the kidneys, there was evidence of cloudy swelling of the tubular epithelium with interstitial nephritis. Plasma cholinesterase activity was reduced in females at all levels of treatment, and in males only at 15 and 50 mg/kg/day. No significant inhibition of red blood cell or brain cholinesterase activities was observed in males or females treated with 5, 1.5 or 0.5 mg/kg/day ronnel (McCollister et al., 1959). These cholinesterase activities were reduced in males and females treated with 15 or 50 mg/kg/day. Red blood cell cholinesterase activity at 15 mg/kg/day was 76% (males) and 71% (females) of control values, and at 50 mg/kg/day was 53% (males) and 50% (females) of control values. Brain cholinesterase activity at 15 mg/kg/day

was 66% (males) and 68% (females) of control values and at 50 mg/kg/day was 39% (males) and 42% (females) of control values.

5.6. OTHER RELEVANT INFORMATION

The following LD₅₀s are given by NIOSH (1983) for ronnel:

oral	rat	906 mg/kg
oral	mouse	2000 mg/kg
oral	rabbit	420 mg/kg
oral	guinea pig	1400 mg/kg
dermal	rat	2000 mg/kg
dermal	rabbit	1000 mg/kg
dermal	guinea pig	2000 mg/kg
intraperitoneal	rat	2823 mg/kg
intraperitoneal	mouse	118 mg/kg
unknown	mammal	400 mg/kg

An oral LD₅₀ for ronnel was 1250 mg/kg in rats (Servintuna, 1963), an oral LD₅₀ in the rabbit for pure ronnel (98.5%) was reported as 462 mg/kg, and the oral LD₅₀ for technical grade ronnel (86.5%) was 272 mg/kg in the rabbit (Kalinowska and Zasadowski, 1977).

Gaines (1969) reported oral LD₅₀s in the rat of 1250 mg/kg for males and 2630 mg/kg for females.

Dietary concentrations of 5, 10 or 30 ppm for 30 days and 10, 30, 100, 300 or 500 ppm for 7 days inhibited liver and plasma carboxyesterases in rats, but had no significant ($p > 0.05$) effect on brain cholinesterase levels. The NOEL for carboxyesterase inhibition in the 30-day feeding study was identified as 5-10 ppm (Murphy and Cheever, 1968). A single intraperitoneal injection of 25, 50, 100 or 200 mg/kg ronnel in corn oil to rats also inhibited the hydrolysis of malathion, diethyl succinate and triacetin by liver and plasma, but had little effect on rat brain and red blood cell cholinesterase activities (Murphy and Cheever, 1968).

Ronnel was found to inhibit the hydrolysis of diethyl succinate and tributyrin by liver and serum, and cholinesterase activity by liver, serum

and brain tissues in rats, fed dietary concentrations of 1, 5 and 25 ppm for 1 week (Su et al., 1971). In an abstract of a Japanese study, Shimamoto and Hattori (1966) also found that an unspecified dose of ronnel, administered orally to rats for 12 weeks, inhibited the cholinesterase activity of erythrocytes, serum, heart, liver, brain and gastrocnemius muscle. Inhibition of acetylcholinesterase activity in rats resulting from oral administration of ronnel was also described in two abstracts of Polish studies by Panek et al. (1973) and Sulinski et al. (1976).

Sitkiewicz et al. (1977) found that concentrations of 1-100 μ M ronnel did not inhibit rat plasma cholinesterase or rat brain acetylcholinesterase activities in vitro. Ronnel in high concentrations (250-500 μ M) significantly reduced the respiratory capacity of rat brain and liver homogenates, and concentrations of 500 μ M inhibited cytochrome oxidase activity by 32% in the brain and 12% in liver homogenate. In contrast to the brain homogenate, ronnel inhibited succinate dehydrogenase activity in the liver homogenate by -22%. Similar results were presented in an abstract of a Polish study. Rakowska et al. (1976) found single and repeated administration of ronnel to rats at several doses (2, 5, 10 and 50% of the LD₅₀) increased the cytochrome oxidase activity in the solubilized brain mitochondrial fractions and 50% of the LD₅₀ decreased the succinate dehydrogenase activity. In an abstract of a Romanian study, Suteu et al. (1974) added ronnel at 1, 10 or 50 ppm to the diet of rats for 4 weeks and found an increase in in vitro oxygen consumption in rat liver, and increased muscle and blood cholinesterase activity.

6. AQUATIC TOXICITY

6.1. ACUTE TOXICITY

The acute toxicity of ronnel has been tested in several species of freshwater fish (Table 6-1). LC_{50} values for 24-, 48- or 96-hour exposures ranged from 0.39-1.17 mg ronnel/l in five species of trout (Willford, 1967; Johnson and Finley, 1980). Brown trout and brook trout were the most susceptible, with 48-hour LC_{50} values of 0.39 and 0.39, respectively (Willford, 1967). The 96-hour LC_{50} values for lake trout, rainbow trout and cutthroat trout were 0.490, 0.550 and 0.555 mg ronnel/l, respectively (Johnson and Finley, 1980). The bluegill sunfish (Lepomis macrochirus) and channel catfish (Ictalurus punctatus) were somewhat more resistant to ronnel exposure, having 24-, 48- and 96-hour LC_{50} values of 2.50, 1.00 and 1.300 mg/l, and 1.76, 1.26 and 1.600 mg/l, respectively (Willford, 1967; Johnson and Finley, 1980). Ronnel applied to ponds containing mosquito fish, Gambusia affinis, at a rate of 0.2 and 0.8 lbs/acre for the control of mosquito larvae was not lethal to the fish within 48 hours (Mulla et al., 1963).

The 24- and 48-hour LC_{50} values for ronnel in juvenile spot, Leiostomus xanthurus, were 0.42 and 0.32 mg/l, respectively (see Table 6-1) (U.S. FWS, 1965). This species, a marine fish, appears more susceptible to ronnel than were the trout.

The 24- and 48-hour EC_{50} values for loss of equilibrium in brown shrimp, Penaeus aztecus, were 0.015 and 0.0052 mg ronnel/l, respectively (U.S. FWS, 1965). The 96-hour EC_{50} for inhibition of shell growth in oysters, Crassostrea virginica, was 0.17 mg/l (U.S. FWS, 1965). The 96-hour LC_{50} for the amphipod, Gammarus fasciatus, was 4.3 mg ronnel/l

TABLE 6-1
Acute LC₅₀ Values of Ronnel to Fish Species

Species	Duration (hours)	LC ₅₀ (mg/l)	Method	Reference
Marine spot, <u>Leiostomus xanthurus</u>	24 48	0.42 0.32	flowthrough flowthrough	U.S. FWS, 1965
Brown trout, <u>Salmo trutta</u>	24 48	0.53 0.39	static static	Willford, 1967
Brook trout, <u>Salvelinus fontinalis</u>	24 48	0.59 0.39	static static	Willford, 1967
Lake trout, <u>Salvelinus namaycush</u>	24 48 96	0.73 0.62 0.490	static static static	Willford, 1967; Johnson and Finley, 1980
Rainbow trout, <u>Salmo gairdneri</u>	24 48 96	1.17 0.74 0.550	static static static	Willford, 1967; Johnson and Finley, 1980
Cutthroat trout, <u>Salmo clarki</u>	96	0.555	static	Johnson and Finley, 1980
Bluegill sunfish, <u>Lepomis macrochirus</u>	24 48 96	2.50 1.00 1.300	static static static	Willford, 1967; Johnson and Finley, 1980
Channel catfish, <u>Ictalurus punctatus</u>	24 48 96	1.76 1.26 1.600	static static static	Willford, 1967; Johnson and Finley, 1980

(Johnson and Finley, 1980). Mulla et al. (1963) reported that 2/20 tadpoles of the toads Bufo boreas and Scaphiopus hammondi exposed to ronnel applied to a pond at 0.2 lbs/acre died within 24 hours. No deaths among tadpoles exposed to 0.8 lbs/acre were reported, however.

6.2. CHRONIC EFFECTS

Pertinent data on the effects of chronic exposure to ronnel in aquatic organisms were not located in the available literature.

6.3. PLANT EFFECTS

Pertinent data on the effects of ronnel to aquatic plants were not located in the available literature.

6.4. RESIDUES

Pertinent data on the residues and occurrence of ronnel in the aquatic environment were not located in the available literature.

6.5. OTHER RELEVANT INFORMATION

Additional data relevant to the toxicity of ronnel in the aquatic environment were not located in the available literature.

7. EXISTING GUIDELINES AND STANDARDS

7.1. HUMAN

The OSHA standard for ronnel in workplace air is 15 mg/m³ as a TWA concentration for an 8-hour workday (29 CFR 1910). The ACGIH (1982) has adopted a TLV-TWA of 10 mg/m³ for ronnel in workroom air.

7.2. AQUATIC

Guidelines and standards for the protection of aquatic organisms from the toxic effects of ronnel were not located in the available literature.

8. RISK ASSESSMENT

Pertinent data regarding the carcinogenicity of ronnel were not located in the available literature, and the limited data on mutagenicity and teratogenicity are inadequate for risk assessment purposes.

The chronic dietary studies of Worden et al. (1972) and McCollister et al. (1959) in rats and dogs can be used for quantitative risk assessment for ronnel. Groups of three male and three female dogs (Pembroke Shire Corgis) and 20 male and 20 female rats were administered doses of ronnel at 1, 3 or 10 mg/kg bw/day and 0.5, 1.5, 5, 15 or 50 mg/kg bw/day, respectively, through the diet for 2 years (Worden et al., 1972; McCollister et al., 1959). At the 3 mg/kg bw/day dose level, the dogs experienced a slight depression in plasma cholinesterase activity; however, the authors noted that this was within a 20% variation of pre-treatment values and did not appear to be of practical significance (Worden et al., 1972). Thus, a NOEL of 3 mg/kg bw/day may be defined for this study. The only effect noted at 10 mg/kg bw/day was a reduction in plasma cholinesterase activity; no overt signs of toxicity were observed and hematologic and histologic parameters were unaffected. A limited experiment by McCollister et al. (1959) provides some corroboration for this value. Plasma cholinesterase was reduced in dogs at 10 mg/kg bw/day, but not at 3 mg/kg bw/day.

No gross signs or microscopic adverse effects were observed in rats at/dose levels of 5 or 15 mg/kg bw/day, while at the 50 mg/kg bw/day dose, histopathologic changes occurred in the liver and kidneys (McCollister et al., 1959). Although plasma cholinesterase activity was inhibited at all dose levels, no significant inhibition of red blood cell or brain cholinesterase activities was observed in male or female rats treated with ≤ 5 mg/kg bw/day. At 15 mg/kg bw/day, both red blood cell and brain cholin-

esterase activities were inhibited, with the greatest inhibition observed in females. Because reductions in red blood cell and brain cholinesterase activities are not, in and of themselves, clearly adverse, and because the animals were not tested for behavioral or neurological effects, it is not clear whether the 15 mg/kg bw/day dosage constitutes a LOAEL or a NOAEL for rats. The 5 mg/kg bw/day dosage clearly is a NOAEL.

The 2-year dietary study in rats (McCollister et al., 1959) is more adequate, in terms of numbers of animals and duration (relative to lifespan), than is the similar study in dogs. Using the NOAEL of 5 mg/kg bw/day from the rat study and an uncertainty factor of 100 (10 to account for interspecies extrapolation and 10 for protection of the most sensitive humans within the population), an ADI of 0.05 mg/kg bw/day, equivalent to 3.5 mg/day for a 70 kg man, can be calculated.

Statements concerning available literature in this document refer to published, quotable sources and are in no way meant to imply that confidential data, which this document could not address, are not in existence. These data, which are considered Confidential Business Information (CBI), are available in summary form as a CBI Appendix that can be accessed by individuals with appropriate clearance. Conclusions from the CBI Appendix regarding risk assessment can, however, be presented in this chapter.

The CBI Appendix to this document reviews other animal and human studies; however, the data do not necessitate a change in the risk assessment.

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APPENDIX: LITERATURE SEARCHED

This profile is based on data identified by computerized literature searches of:

CA SEARCH (Files 308, 309, 310, 311, 320)
TOXLINE
MEDLINE
RTECS
SCI SEARCH
OHM TADS
STORET
SRC Environmental Fate Data Bases
SANSS
AQUIRE

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